AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions of claims in the application.

LISTING OF CLAIMS:

1. (Original) An aldehyde having the formula:

$$\begin{array}{c} \textbf{RO-PAG-O(CH_2)_z(Y)_m-C-X(CH_2)_wCHO} \\ \textbf{0} \end{array}$$

IA

wherein R is hydrogen or lower alkyl, X and Y are individually selected from -O - or - NH- with the proviso that X is NH when m is 1 and Y is -O-, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups and having a molecular weight of from about 1,000 to about 100,000 Daltons, z is an integer of from 2 to 4, m is an integer of from 0 to 1, and w is an integer of from 2 to 8, wherein the aldehyde group is free or protected with a hydrolyzable aldehyde protecting group, or a hydrate thereof.

- 2. (Original) The aldehyde of claim 1 wherein said residue is formed from polyethylene glycol.
- 3. (Original) The aldehyde of claim 2 wherein the residue has a molecular weight of 5,000 to 50,000 Daltons.
- 4. (Original) The aldehyde of claim 1 wherein said aldehyde has a formula:

RO-PAG-O(CH₂)_z-C-NH-(CH₂)_wCHO

I-Ai

wherein R, PAG, and w are as above, and z is an integer of from 1 to 4

- 5. (Original) The aldehyde of claim 4 wherein said divalent residue is polyethylene glycol.
- 6. (Original) The aldehyde of claim 5 wherein the residue has a molecular weight of 5,000 to 50,000 Daltons.
- 7. (Original) The aldehyde of claim 6 wherein R is methyl and the molecular weight of the residue is about 10,000 Daltons.
- 8. (Original) The aldehyde of claim 6 wherein R is methyl, and the molecular weight of the residue is 20,000 Daltons.
- 9. (Original) The aldehyde of claim 1 wherein said aldehyde has the formula:

$$RO$$
-PAG-O(CH_2)_zOCNH(CH_2)_wCHO

I-Aii.

wherein R, PAG, and w are as above, and z is an integer of from 2 to 4

10. (Original) The aldehyde of claim 9 wherein said divalent residue is formed from polyethylene glycol.

- 11. (Original) The aldehyde of claim 10 wherein the residue has a molecular weight of 5,000 to 50,000 Daltons.
- 12. (Original) The aldehyde of claim 11 wherein R is methyl and said residue has a molecular weight of 10,000 Daltons.
- 13. (Original) The aldehyde of claim 1 having the formula:

$$\begin{array}{c} \textbf{RO-PAG-O(CH_2)_zNH-C-NH-(CH_2)_wCHO} \\ \textbf{0} \end{array}$$

I-Aiii

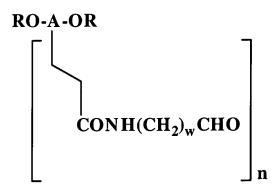
wherein R, PAG, and w are as above, and z is an integer of from 2 to 4.

- 14. (Original) The aldehyde of claim 13 wherein said divalent residue is polyethylene glycol.
- 15. (Original) The aldehyde of claim 14 wherein the residue has a molecular weight of 5,000 to 50,000 Daltons.
- 16. (Original) The aldehyde of claim 15 wherein R is methyl and the molecular weight of the residue is 10,000 Daltons.
- 17. (Original) The aldehyde of claim 1 having the formula:

wherein R, PAG, and w are as above, and z is an integer of from 2 to 4.

18. (Original) The aldehyde of claim 17 wherein said divalent residue is formed from polyethylene glycol.

- 19. (Original) The compound of claim 18 wherein the residue has a molecular weight of 5,000 to 10,000 Daltons.
- 20. (Original) The aldehyde of claim 19 wherein R is methyl and the molecular weight of the residue is 10,000 Daltons.
- 21. (Original) An aldehyde of the formula:



IB

wherein R is hydroxyl or lower alkyl, A is a polyethylene glycol residue with its two terminal hydroxy groups being removed having a molecular weight of from 1,000 to 100,000 Daltons and having a valence of from 1 to 5, n is an integer of from 1 to 5 which integer is the same as the valence of A, and w is an integer from 2 to 8.

- 22. (Original) The aldehyde of claim 21 wherein A is a residue having a molecular weight of from 5,000 to 50,000 Daltons.
- 23. (Original) The aldehyde of claim 22 where n is 1.
- 24. (Original) The aldehyde of claim 23 where the R is methyl and A has a molecular weight of about 20,000 Daltons.

- 25. (Original) The aldehyde of claim 23 wherein R is methyl and A has a molecular weight of 10,000 Daltons.
- 26. (Original) An aldehyde of the formula:

$$\begin{array}{c} \text{O-PAG}^2\text{-OR}^1\\ \text{O} \quad (\text{CH}_2)_p\\ \text{RO-PAG}^1\text{-O(CH}_2)_z\text{-O-C-NH-CH-CONH(CH}_2)_w\text{CHO} \end{array}$$

IC

wherein PAG¹ and PAG² are independently divalent residues of poly lower alkylene glycol resulting from removal of the two terminal hydroxy groups with the PAG¹ and PAG² residues having a combined molecular weight of from 1,000 to 100,000 Daltons, R and R¹ are individually lower alkyl or hydrogen, z is an integer of from 2 to 4, p is an integer of from 2 to 5, and w is an integer of from 2 to 8, wherein the aldehyde group is free or protected with a hydrolyzable aldehyde protecting group, or a hydrate thereof.

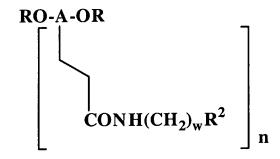
- 27. (Original) The aldehyde of claim 26 wherein said R is methyl, PAG¹ and PAG² are formed from polyethylene glycol residues.
- 28. (Original) The aldehyde of claim 27 wherein R is methyl and PAG¹ and PAG² both have a molecular weight of 5,000 to 50,000 Daltons.
- 29. (Original) A compound of the formula:

wherein R is hydrogen or lower alkyl, R² is CH(OH)CH(OH)R₁₃ wherein R₁₃ is hydrogen, alkyl, or
phenyl, X and Y are individually selected from -O- or -NHwith the proviso that X is NH when m is 1 and Y is -O-, PAG
is a divalent residue of polyalkylene glycol resulting from
removal of the terminal hydroxy groups and having a
molecular weight of from about 1,000 to about 100,000
Daltons, z is an integer of from 2 to 4, m is an integer of from
0 to 1, and w is an integer of from 2 to 8.

30. (Original) The conjugate of claim 29 where said conjugate has the formula:

wherein PAG, R, R², z and w are as above.

31. (Original) A compound of the formula:



wherein R is hydrogen or lower alkyl, R^2 is - $CH(OH)CH(OH)R_{13}$ wherein R_{13} is hydrogen, alkyl, or phenyl, A is a polyethylene glycol residue with its two terminal hydroxy groups being removed having a molecular weight of from 1,000 to 100,000 Daltons and having a valence of from 1 to 5, n is an integer of from 1 to 5 which integer is the same as the valence of A, and w is as integer of from 2 to 8.

32. (Original) A compound of the formula:

$$\begin{array}{c} \text{O-PAG}^2\text{-OR}^1\\ \text{O} \quad (\text{CH}_2)_p\\ \parallel \quad \mid \\ \text{RO-PAG}^1\text{-O(CH}_2)_z\text{-O-C-NH-CH-CONH(CH}_2)_wR^2 \end{array}$$

wherein PAG¹ and PAG² are independently divalent residues of poly lower alkylene glycol resulting from removal of the two terminal hydroxy groups with the PAG¹ and PAG² residues having a combined molecular weight of from 1,000 to 100,000 Daltons, R and R¹ are individually lower alkyl or hydrogen, R² is CH(OH)CH(OH)R₁3 wherein R₁3 is hydrogen, alkyl, or phenyl, w is an integer from 2 to 8, p is an integer of from 2 to 5, and z is an integer of from 2 to 4.

33. (Original) A compound of the formula:

RO-PAG-O(CH_2)_z-O-(CH_2)_w- R^2

wherein R is lower alkyl or hydrogen, R^2 is - $CH(OH)CH(OH)R_{13}$ wherein R_{13} is hydrogen, alkyl, or phenyl, PAG is the divalent residue of polyethylene glycol resulting from removal of the two terminal hydroxy groups having a molecular weight of from 1,000 to 100,000 Daltons, z is a integer of from 2 to 4 and w is an integer of from 2 to 8.

34. (Original) A conjugate of the formula:

$$\begin{array}{c} \text{RO-PAG-O(CH$_2$)}_{z}(Y)_{m}\text{-C-X-(CH$_2$)}_{w}\text{CH$_2$NHP} \\ \parallel \\ \text{O} \end{array}$$

III-A

wherein P is the residue of a protein with its amino group removed, R is hydrogen or lower alkyl, X and Y are individually selected from -O- or -NH with the proviso that X is NH when Y is -O-, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups, having a molecular weight of from 1,000 to 100,000 Daltons, z is an integer of from 2 to 4, m is an integer of from 0 to 1, and w is an integer of from 2 to 8.

35. (Original) The conjugate of claim 34 where said conjugate has the formula:

RO-PAG-O(CH_2)_z-C-NH-(CH_2)_w CH_2 NHP

III-E

wherein P, R, PAG, z and w are as above.

- 36. (Original) The conjugate of claim 35 wherein PAG is formed from polyethylene glycol having a molecular weight of from 5,000 to 50,000.
- 37. (Original) The conjugate of claim 36 where said P is G-CSF, EPO, IFN- α , IFN- β or Hemoglobin.
- 38. (Original) The conjugate of claim 34 wherein said conjugate has the formula:

III-F

wherein P, R, PAG, and w are as above, and z is an integer of from 2 to 4.

- 39. (Original) The conjugate of claim 38 wherein PAG is polyethylene glycol having a molecular weight of from 5,000 to 50,000.
- 40. (Original) The conjugate of claim 39 where said P is G-CSF, EPO, IFN- α , IFN- β or Hemoglobin.
- 41. (Original) The conjugate of claim 34 wherein said conjugate has the formula:

$$\begin{array}{c} \textbf{RO-PAG-O(CH_2)_zNH-C-NH-(CH_2)_wCH_2NHP} \\ \parallel \\ \textbf{O} \end{array}$$

III-G

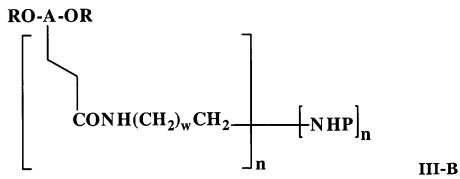
wherein P, R, PAG, and w are as above, and z is an integer of from 2 to 4.

- 42. (Original) The conjugate of claim 41 wherein PAG is polyethylene glycol having a molecular weight of from 5,000 to 50,000.
- 43. (Original) The conjugate of claim 42 where said P is G-CSF, EPO, IFN- α , IFN- β or Hemoglobin.
- 44. (Original) The conjugate of claim 34 wherein said conjugate has the formula:

III-H

wherein P, R, PAG, and w are as above, and z is an integer of from 2 to 4.

- 45. (Original) The conjugate of claim 44 wherein PAG is polyethylene glycol having a molecular weight of from 5,000 to 50,000 Daltons.
- 46. (Original) The conjugate of claim 45 where said P is G-CSF, EPO, IFN- α , IFN- β or hemoglobin.
- 47. (Original) A conjugate of the formula:



#821760 v1 103095-41585 wherein P is a residue of a protein with its amino group removed, R is hydrogen or lower alkyl, A is a polyethylene glycol residue with its two terminal hydroxy groups being removed having a molecular weight of from 1,000 to 100,000 Daltons and having a valence of from 1 to 5, n is an integer of from 1 to 5 which integer is the same as the valence of A, and which integer is the same as the number of proteins P, w is as above.

- 48. (Original) The conjugate of claim 47 where n is 1.
- 49. (Original) The conjugate of claim 47 where A is polyethylene glycol residue.
- 50. (Original) The conjugate of claim 49 wherein PAG is polyethylene glycol having a molecular weight of from 5 to 50,000 Daltons.
- 51. (Original) A conjugate with the formula:

$$\begin{array}{c} O\text{-PAG}^2\text{-OR}^1\\ O \quad (CH_2)_p\\ \parallel \quad \mid \\ RO\text{-PAG}^1\text{-O}(CH_2)_z\text{-O-C-NH-CH-CONH}(CH_2)_wCH_2NHP \end{array}$$

III-C

wherein P is a residue of a protein with its amino group being removed, PAG¹ and PAG² are independently divalent residues of poly lower alkylene glycol resulting from removal of the two terminal hydroxy groups and with the PAG¹ and

PAG² residues having a combined molecular weight of from 1,000 to 100,000 Daltons, R and R¹ are individually lower alkyl or hydrogen, w is an integer of from 2 to 8, p is an integer of from 2 to 5, and z is an integer of from 2 to 4.

- 52. (Original) The conjugate of claim 51 where PAG¹ and PAG² are each polyethylene glycol having a combined molecular weight from 5,000 to 50,000.
- 53. (Original) A conjugate of the formula:

RO-PAG-O(CH₂)_zO-(CH₂)_wCH₂NHP

III-D

wherein P is a residue of a protein with an amino group being removed, PAG is a divalent residue of a poly lower alkylene glycol resulting from removal of the two terminal hydroxy groups having a molecular weight of from 1,000 to 100,000 Daltons, R is lower alkyl or hydrogen, w is an integer from 2 to 8 and z is an integer from 2 to 4.

- 54. (Original) The conjugate of claim 53 where PAG is a polyethylene glycol residue.
- 55. (Original) The conjugate of claim 54 where PAG has a molecular weight of from 5,000 to 50,000 Daltons.
- 56. (Original) A process for producing an aldehyde of the formula:

$$RO-PAG-O-(CH_2)_z-O-(CH_2)_w-CHO$$

wherein R is lower alkyl, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal

hydroxy groups, having a molecular weight of from 1,000 to 100,000 Daltons, z is an integer of from 2 to 4, and w is an integer of from 2 to 8;

from a hydroxy compound of the formula

RO-PAG-O-(CH₂)_z-OH

wherein R, PAG are as above, and z is an integer of from 2 to 4; comprising esterifying said hydroxy compound to form an ester of the formula;

RO-PAG-O-(CH₂)_z-OL

wherein R and PAG are as above and OL is a sulfonic acid ester;

by reacting said hydroxy compound with a sulfonating agent having the formula

HaloL

wherein L is a sulfonyl leaving group and Halo is a halogen; to form said sulfonate ester, and reacting said ester with an acetonide of the formula

wherein R_{13} is hydrogen, alkyl, or phenyl, w is as above and B is an alkali metal;

to form a polymeric acetonide of the formula

RO-PA G-O-
$$(CH_2)_z$$
-O $(CH_2)_w$ R_{13}

wherein R, PAG, R₁₃, z and w are as above;

and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation with a periodate oxidizing agent to form said aldehyde.

57. (Original) A process for producing an aldehyde of the formula:

wherein R is lower alkyl, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups, having a molecular weight of from 1,000 to 100,000 Daltons, z is an integer of from 2 to 4, and w is an integer of from 2 to 8;

from a hydroxy compound of the formula

RO-PAG-O-(CH₂)_z-OH

wherein R, PAG and z are as above; comprising halogenating said hydroxy compound to form a halide of the formula

RO-PAG-O-(CH₂)_z-X

by reacting said hydroxy compound with a halogenating agent having the formula

X_2SO

wherein X is a halogen;

to form said halide, and reacting said halide with an acetonide of the formula

$$BO \longrightarrow (CH_2)_W \longrightarrow R_{13}$$

wherein R_{13} is hydrogen, alkyl, or phenyl, w is as above and B is an alkali metal;

to form a polymeric acetonide of the formula

RO-PA G-O-
$$(CH_2)_z$$
-O $(CH_2)_w$ R_{13}

wherein R, R₁₃, PAG, z and w are as above;

and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation with a periodate oxidizing agent to form said aldehyde.

58. (Original) A process for producing an aldehyde of the formula:

RO-PEG-O-(CH₂)_z-O-(CH₂)_w-CHO

wherein PEG is a divalent residue of polyethylene glycol resulting from removal of the terminal hydroxy groups, having a molecular weight of from 1,000 to 100,000 Daltons, and w is an integer of from 2 to 8, and z is an integer of from 2 to 4

from an acetonide of the formula

$$R_{13}$$

wherein B is an alkali metal, and R_{13} and w are as above; comprising reacting said acetonide with ethylene oxide by passing liquid ethylene oxide into an organic solution containing the acetonide under polymerization conditions to form

HO-PEG-O-
$$(CH_2)_z$$
-O- $(CH_2)_w$ R_{13}

wherein PEG, R_{13} , z and w are as above;

the hydroxy acetonide compound of the formula

etherifying said hydroxy acetonide with a lower alkyl halide to form a polymeric acetonide of the formula

RO-PEG-O-
$$(CH_2)_z$$
-O $(CH_2)_w$ R_{13}

wherein R is lower alkyl, and PEG, R_{13} , z and w are as above;

and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation with a periodate oxidizing agent to form said aldehyde.

59. (Original) A process for producing an aldehyde of the formula:

$$RO$$
-PEG-O-(CH_2)_z-O-(CH_2)_w-CHO

wherein PEG is a divalent residue of polyethylene glycol resulting from removal of the terminal hydroxy groups, having a molecular weight of from 1,000 to 100,000 Daltons, z is an integer of from 2 to 4, and w is an integer of from 2 to 8;

from a polymeric acetonide of the formula

RO-PEG-O-
$$(CH_2)_z$$
-O $(CH_2)_w$ R_{13}

wherein R, PEG, R₁₃, z and w are as above;

and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation with a periodate oxidizing agent to form said aldehyde.

Claims 60-63. (Canceled)

64. (Original) The conjugate of the formula:

$$\begin{array}{c} \text{RO-PAG-OCH}_2\text{-C-NH-(CH}_2)_\text{w}\text{CH}_2\text{NHP} \\ \parallel \\ \text{O} \end{array} \qquad \qquad \text{I-Ai}$$

wherein R is hydrogen or lower alkyl, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups and having a molecular weight of from 1,000 to 100,000 Daltons, and w is an integer of from 2 to 8.

- 65. (Original) The aldehyde of claim 64 wherein said divalent residue is polyethylene glycol.
- 66. (Original) The aldehyde of claim 65 wherein the residue has a molecular weight of 5,000 to 50,000 Daltons.

- 67. (Original) The aldehyde of claim 66 wherein R is methyl, and the molecular weight of the residue is about 10,000 Daltons.
- 68. (Original) The aldehyde of claim 67 wherein R is methyl, and the molecular weight of the residue is about 20,000 Daltons.
- 69. (Original) The conjugate of the formula:

$$\begin{array}{c} \text{RO-PAG-OCH}_2\text{-C-NH-(CH}_2)_wR_2 \\ \parallel \\ \text{O} \end{array}$$

wherein PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups and having a molecular weight of from 1,000 to 100,000 Daltons, R is lower alkyl or hydrogen, R^2 is $CH(OH)CH(OH)R_{13}$ wherein R_{13} is hydrogen, alkyl, or phenyl, and w is an integer of from 2 to 8 and are as above.

70. (Original) The conjugate of the formula:

III-E

wherein P is a residue of a protein with its amino group being removed, R is hydrogen or lower alkyl, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups, having a combined molecular

weight of from 1,000 to 100,000 Daltons, w is an integer of from 2 to 8 and are as above.

- 71. (Original) The conjugate of claim 70 wherein PAG is formed from polyethylene glycol having a molecular weight of from 5,000 to 50,000
- 72. (Original) The conjugate of claim 70 where P is G-CSF, EPO, IFN- α , IFN- β or Hemoglobin.
- 73. (Original) A compound of the formula:

$$O-PAG-OR^1$$

$$(CH_2)_p$$

$$O+PAG-OR^1$$

$$(CH_2)_p$$

$$O+PAG-OR^1$$

$$O+PAG-OR^1$$

$$O+PAG-OR^1$$

$$O+PAG-OR^1$$

$$O+PAG-OR^1$$

$$O+PAG-OR^1$$

wherein R¹ is lower alkyl, or hydrogen, PAG is a divalent residue of polyalkylene glycol resulting from removal of the terminal hydroxy groups, having a combined molecular weight of from 1,000 to 100,000 Daltons, and p is an integer of from 2 to 5.

74. (Original) The conjugate of claim 73 wherein PAG is formed from polyethylene glycol having a molecular weight of from 5,000 to 50,000.